IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Stern et al.	Art Unit	: 1641
Serial No.	: 10/823,866	Examiner	: Unsu Jung
Filed	: April 14, 2004	Conf. No.	: 6194
Title	: MAJOR HISTOCOMPATIBILITY COMPLEX (MHC)-PEPTIDE ARRAYS		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF LAWRENCE J. STERN, PH.D.

I, Lawrence J. Stern, Ph.D., residing at 4 Captain Brown's Lane, Acton, Massachusetts, hereby declare that:

1. I am a Professor at the University of Massachusetts Medical School, with appointments in the Departments of Pathology and Biochemistry and Molecular Pharmacology. A copy of my curriculum vitae is attached as Exhibit A.

2. I am familiar with the present claims of the application, which are directed to, inter alia, arrayscomprising (i) a flat substrate, (ii) anti-factor antibodies specific for secreted factors immobilized on the substrate, and (iii) a plurality of MHC molecules complexed with antigen-derived peptides immobilized in spatially-distinct areas on the substrate, and further comprising at least one hydrophobic barrier that surrounds a plurality of said spatially-distinct areas; and each of said spatially-distinct areas is not surrounded individually by a separate hydrophobic barrier, such that when a single volume of sample is applied inside of the at least one hydrophobic barrier, all areas in the plurality of said spatially-distinct areas are in contact with the single volume of sample, and wherein at least one of the spatially-distinct areas comprises a plurality of MHC-peptide complexes that are different from the MHC-peptide complexes of at least one other spatially-distinct area..

3. I have reviewed the Office Action mailed May 12, 2009, and am familiar with the rejections contained therein. In particular, I note that the Examiner alleges that the pending claims are obvious over a number of cited references. I have also reviewed those cited references. I disagree with the rejection.

4. The activation of T cells by MHC-peptide complexes has been extensively studied since its discovery and is considered one of the best-understood areas of molecular

immunology. T cells interact with the immobilized MHC-peptide complexes via their T antigen receptor (TCR), and this interaction stimulates the cells, initiating a complex series of intracellular signaling pathways that eventually lead to cytokine secretion (Ullman 1990; copy attached). The MHC-TCR interaction is transient, with dissociation lifetimes of about 10-100 sec (Fremont 1996, Davis 1998, vanderMerwe 2003; copies attached). The lifetime of costimulatory interactions is even shorter, often <1 sec (vanderMerwe 2003). Contrast these times with the much longer time taken for T cell activation and initiation of cytokine secretion (Ullman 1990, Lanzavecchia 2000; copy attached). While the initial T cell intracellular signaling events such as kinase activation and receptor phosphorylation take place in seconds to minutes, the multiplicity of signaling pathways and the complexes of intracellular signal processing lead to many rate limiting steps in the overall activation process. Cytokine secretion is at or near the end of this process (Ullman 1990). Cytokine secretion typically is not assayed until ~12 hrs post stimulation.

5. During the hours between initial TCR engagement and detection of cytokine secretion, the activated T cells would not be expected to stay in the same region of the array. T cells are not anchorage dependent and live as isolated cells in suspension both in vivo and in vitro. They are well known to be highly mobile, and readily move from cell-to-cell in the body and on surfaces. In the case of T cell activation by an intact antigen presenting cell, T cell mobility arrest can occur, but this process requires a constellation of adhesion molecules on the surface of the antigen presenting cell, and lateral mobility of MHC molecules on the APC surface, so that they can follow TCR molecules as they are driven into an immunological synapse. However, the interaction of T cells with immobilized MHC molecules involves neither adhesion molecules nor MHC mobility, would not be expected to induce T cell mobility arrest. Thus, T cells would be expected to move over the array during the course of the assay, with cytokine secretion occurring outside the areas of immobilized MHC-peptide complexes, with the expected result being high background signals and captured cytokine signals not aligned with the spatially-distinct areas of the array.

6. In addition to movement of T cells during the course of the assay, the secreted cytokines also are mobile. Cytokines are relatively small proteins with molecular weights of about 25,000. Diffusion coefficients for these proteins have been experimentally measured (for

example 9.5 x $10^{-7}cm^2sec^{-1}$) and these measurements are consistent with theoretical understanding of diffusion processes. The relationship between diffusion coefficients and average molecular displacement is well understood and described by Frick's Law: the characteristic distance moved by a molecule of diffusion constant D in time t is 2*sqrt(Dt). For a molecule with D=9.5x$10^{-7}cm^2sec^{-1}$, the theoretical characteristic diffusion distance for 12 hours is 6.9 mm, and for 4 hours is 2.3 mm. These distances would be significantly increased in any actual device due to unavoidable vibration and thermal convection processes. These characteristic diffusion distances are large relative to the sizes and spacing of the spatially-distinct areas that are conventionally used (for example, the spots on such arrays can typically be about 0.05 to 0.5 mm wide, spaced about 0.1 to 1 mm apart), and would be expected to result in a very high background staining such that individual areas would be indistinguishable.

7. Thus, for at least these reasons, one of skill in the art would not have had a reasonable expectation that the claimed arrays described would work; surprisingly, as shown in the Examples set forth in the present application, the arrays do work, and give clear, reproducible results that can detect very rare T cells.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, under Title 18 § 1001 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

11.12.09
Date

Lawrence J. Stern, Ph.D.

Kathleen V. Bateman - notary public
my commission expires 10/3/2014

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My Commission Expires
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Curriculum Vitae - LAWRENCE J. STERN

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Education:

B. A. *cum laude*	Chemistry	Cornell University (1983)
Ph. D.	Biochemistry	Massachusetts Institute of Technology (1989)

Professional Experience:

2005-present Professor of Pathology and Biochemistry
2002-2005 Associate Professor of Pathology and Biochemistry
University of Massachusetts Medical School
Departments of Pathology and Biochemistry & Molecular Pharmacology
Mechanisms of Antigen Presentation and Response in the Immune System

1999-2002 Associate Professor of Chemistry
1997-2002 Member, Center for Biomedical Engineering
1994-1999 Assistant Professor of Chemistry
Massachusetts Institute of Technology, Department of Chemistry
Structure and Function of Immune Receptors

1989-1994 Postdoctoral Fellow (with Don. C. Wiley)
Harvard University, Department of Biochemistry and Molecular Biology
Structural Studies of MHC Proteins

1983-1989 Graduate Research Assistant (with H. Gobind Khorana)
Massachusetts Institute of Technology, Department of Chemistry
Structure-Function Studies of Bacteriorhodopsin

1981-1983 Undergraduate Research Student (with Lawrence Que, Jr.)
Cornell University, Department of Chemistry
Mechanism of Catechol Dioxygenases

Honors and Awards:

2009 Faculty Achievement Award
1997 Pfizer-Laubach Career Development Chair
1995 NSF Faculty Early Career Development Award
1992 HHMI Postdoctoral Associate
1989 Damon-Runyon Walter Winchell Cancer Research Fellow
1986 NIH Predoctoral Trainee

Patents

Empty Major Histocompatibility Class II Heterodimers (5,583,031) 12/10/1996
Immunomodulatory Peptides (5,880,103 and 5,827,576.) 10/27/1998
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Publications

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J.L. Schmitke, L.J. Stern, A.M. Klibanov
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from Harvard - postdoctoral work

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21. The role of arginines 82 and 227 in the bacteriorhodopsin proton pump.
L.A. Drachev, A.D. Kaulen, H.G. Khorana, T. Mogi, N.V. Postanogova, V.P. Skulachev, and L.J. Stern.
Photochem. PhotoBiol (1992), **55**, 741-744.

20. Effects of individual genetic substitutions of arginine residues on the protonation and reprotonation kinetics of the Schiff base during the bacteriorhodopsin photocycle.
G.C. Lin, M.A. El-Sayed, T. Marti, L.J. Stern, T. Mogi, H.G. Khorana.
Biophys. J. (1991), **60**, 172-178.

19. Substitution of amino acids Asp-85, Asp-212, and Arg-82 in bacteriorhodopsin affects the proton release phase of the pump and the pK of the Schiff base.
H. Otto, T. Marti, M. Holz, T. Mogi, L.J. Stern, F. Engel, H.G. Khorana, M.P. Heyn.
Proc. Natl. Acad. Sci. USA (1990), **87**,1018-1022.

18. Vibrational spectroscopy of bacteriorhodopsin mutants: Evidence of the interaction of proline-186 with the retinylidene chromophore.
K.J. Rothschild, Y.-W. He, T. Mogi,, T. Marti, L.J. Stern, H.G. Khorana.
Biochemistry (1990), **29**, 5954-5960.

17. Effect of genetic modification of tyrosine-185 on the proton pump and the blue-to-purple transition of bacteriorhodopsin.
D.-J. Jang, M.A. El-Sayed, L.J. Stern, T. Mogi, H.G. Khorana.
Proc. Natl. Acad. Sci. USA (1990), **87**, 4103-4107.

16. Sensitivity of the retinal circular dichroism of bacteriorhodopsin to the mutagenic single substitutions of amino acids: tyrosine.
D.-J. Jang, M.A. El-Sayed, L.J. Stern, T. Mogi, H,.G. Khorana
FEBS Lett. (1990), **262**, 155-159.

15. Structure and thermal stability of monomeric bacteriorhodopsin in mixed detergent/phospholipid micelles.
C.G. Brouillette, R.B. McMichens, L.J. Stern, H.G. Khorana
Proteins: Structure, Function, and Genetics (1989), **5**, 38-46.

14. Structure-function studies on bacteriorhodopsin, X. Individual substitutions of arginine residues by glutamine affect chromophore formation, photocycle, and proton translocation.
L.J. Stern and H.G. Khorana
J. Biol. Chem. (1989), **264**, 14202-14208.

13. Conserved amino acids in the F-helix of bacteriorhodopsin form part of a retinal binding pocket.
K.J. Rothschild, M.S. Braiman, T. Mogi, L.J. Stern, H.G. Khorana
FEBS Lett. (1989), **250**, 448-452.

12. Vibrational spectroscopy of bacteriorhodopsin mutants: Chromophore isomerization perturbs tryptophan-86.
K.J. Rothschild, D. Gray, T. Mogi, T. Marti, M.S. Braiman, L.J. Stern, H.G. Khorana
Biochemistry (1989), **28**, 7052.

11. Structure-function studies on bacteriorhodopsin, VIII. Substitutions of the membrane-embedded prolines 50, 91, and 186. The effects are determined by the substituting amino acid.
T. Mogi, L.J. Stern, B.H. Chao, H.G. Khorana
J. Biol. Chem. (1989), **264**, 14192-14196.

10. Substitution of amino acids in helix F of bacteriorhodopsin: Effects on the photochemical cycle.
P.L. Ahl, L.J. Stern, Mogi, T., H.G. Khorana, K.J. Rothschild
Biochemistry (1989), **28**, 10028-10034.

9. Substitution of membrane-embedded aspartic acids in bacteriorhodopsin causes specific changes in different steps of the photochemical cycle.
L.J. Stern, P.L. Ahl, T. Marti, T. Mogi, M. Dunach, S. Berkowitz, K.J. Rothschild, H.G. Khorana
Biochemistry (1989), **28**, 10035-10042.

8. Aspartic acid substututions affect proton translocation by bacteriorhodopsin.
T. Mogi, L.J. Stern, T. Marti, B.H. Chao, H.G. Khorana
Proc. Natl. Acad. Sci. USA (1988), **85**, 4149-4152.

7. Vibrational spectroscopy of bacteriorhodopsin mutants, I. Tyrosine-185 protonates and deprotonates during the photocycle.
M.S. Braiman, T. Mogi, L.J. Stern, N.R. Hackett, B.H. Chao, H.G. Khorana K.J. Rothschild
Proteins: Structure, Function, and Genetics (1988), **3**, 219-229.

6. Effects of amino acid substitutions in the F helix of bacteriorhodopsin: Low temperature UV-visible difference spectroscopy.
P.L. Ahl, L.J. Stern, D. During, H.G. Khorana, K.J. Rothschild
J. Biol. Chem. (1988), **263**, 13594-13601.

5. Vibrational spectroscopy of bacteriorhodopsin mutants: Light-driven proton transport involves protonation changes of aspartic acid residues 85, 96, and 212.
M.S. Braiman, T. Mogi, T. Marti, L.J. Stern, H.G. Khorana, K.J. Rothschild
Biochemistry (1988), **27,** 8516-8520.

4. Structure-function studies on bacteriorhodopsin, IV. Purification and renaturation of bacterio-opsin polypeptide expressed in *E. coli* .
M.S. Braiman, L.J. Stern, B.H. Chao, H.G. Khorana
J. Biol. Chem. (1987), 262, 9721-9276.

3. Structure-function studies on bacteriorhodopsin, V. Effects of amino acid substitutions in the putative helix F.
N.R. Hackett, L.J. Stern, B.H. Chao, K.A. Kronis, H.G. Khorana
J. Biol. Chem. (1987), **262**,9277-9284.

2. Bacteriorhodopsin mutants containing single Tyr to Phe substitutions are all active in proton translocation.
T. Mogi, L.J. Stern, N.R. Hackett, H.G. Khorana
Proc. Natl. Acad. Sci. (1987), **84**, 5595-5599.

from Cornell - undergraduate work

1. Model studies of iron-tyrosinate proteins.
J.W. Pyrz, A.L. Roe, L.J. Stern, L. Que, Jr.
J. Am. Chem. Soc. (1985), **107,** 614-620.

Professional Activities

Study sections and grant review

Ad-hoc reviewer, NSF research and CAREER grants, 1995-2001
Ad-hoc member, NIH special emphasis panels, June 1998, October 2003
Temporary member, NIH study section CMI-A, 2004, 2005, 2008, CMI-B 2008, 2009
Temporary member, NIH study sections ALY and IMB, 1996, 1998, 2001-2003
Chair, Special Emphasis Panel on Immune Epitope Database, February 2003.
NIH RFP review committees, May 1994, Sept. 2001, March 2004, May 2004.
Human Frontier Science Program
Welcome Trust
Cornell High Energy Synchrotron Source
Israel Science Foundation

Scientific Advisory Boards

NIH Epitope Discovery Program, 2004-present

UMass Medical School Committees and Service

Graduate Council (Chair, 2006-2007)
Biological Computing Committee
Senior Scholars Coordinating Committee
Research Retreat Steering Committee

UMass Medical School Programs

Immunology and Virology Graduate Program
Biochemistry and Molecular Pharmacology Graduate Program
Interdisciplinary Graduate Program
Center for AIDS Research
Diabetes and Endocrine Research Center

Manuscript review

Advisory Editor: *J. Exp. Med.* (1994-1997)
Ad-hoc Review: *Science, Immunity, PNAS, J. Exp. Med., Biochemistry, J. Mol. Biol., J. Biol. Chem., Protein Science, Proteins: Struct, Funct. Genetics, Blood, , J. Struct. Biol., J. Immunol. Immunology, Eur. J. Immunol., Int. Immunol., Human Immunol., J. Immunol. Meth., Int. J. Cancer, Immulogy Letters, Annals of Biomed. Engineering BioMedCentral Immunol.,*

Professional Societies

American Chemical Society
American Society for Biochemistry and Molecular Chemistry
International Union of Crystallography
American Association of Immunologists
American Society for the Advancement of Science

Grant Support

Continuing Projects

Cellular Immunity to Class A-C viruses
Principal Investigator: Francis Ennis (UMass) Period: 4/1/09 – 3/31/14 $540,000
Agency: NIH / NIAID Type: Cooperative Agreement (U19-AI57319)
The goal of the Technical Development Component (Stern, P.I.) of this project will be to develop new technologies for the rapid identification of T cell epitopes derived from category A-C viruses and for the analysis of antigen-specific T cells in human peripheral blood samples.

Interaction of HIV Nef with its receptor binding partners
Principal Investigator: Lawrence J. Stern Period: 7/15/07 – 6/30/09 $135,000
Agency: NIH / NIAID Type: Phased Innovation Grant (R21-AI074616)
The goals of this project are to characterize the interaction of HIV Nef with the cytoplasmic domain of TCRzeta and other cell surface receptors. The R21 phase (years 1 and 2) includes the refinement of tools for structural characterization of Nef-target interactions using the TCR zeta system as a test case. The R33 phase includes evaluation of the functional outcome of Nef-TCR zeta interaction, and extension to CD4, MHC class I, CD1, and CD28 cytoplasmic domains.

Structural Studies of Class II MHC Proteins
Principal Investigator: Lawrence J. Stern Period: 2/28/08 - 3/31/13 $250,000
Agency: NIH / NIAID Type: Research Project (R01-AI38996-11)
The goals of the project are to determine the structure and mechanistic basis for the action of the antigen processing components ERAP1 and HLA-DO, and to investigate the role of a hairpin turn in a class II MHC-bound peptide antigen.

Class II MHC Antigen Processing in Dendritic Cells
Principal Investigator: Lawrence J. Stern Period: 2/01/08 - 1/31/13 $250,000
Agency: NIH / NIAID Type: Research Project (RO1-A148833-07)
The goals of this project are to characterize class II MHC antigen loading pathways, to evaluate possible functional roles for empty/open class II MHC molecules, and to define the structural characteristics of the open/empty form of class II MHC proteins.

MHC Array T Cell Assay System for Monitoring Immune Status in Type 1 Diabete
Principal Investigator: E. Guignon (Cienca, Inc.) Period: 5/1/07 – 4/30/09 $9,231
Agency: NIH/NIDDKD Subcontract Type: Small Business Innov (R43-DK-77291-02)
The goal of this research subcontract is to develop test systems for benchmarking grating-coupled surface plasmon resonance-based microarray technology.

Completed projects

Functional HLA-A*0201-peptide and DR0401-peptide microarrays for Type I diabetes
Principal Investigator: W. Kwok (Benaroya Res. Inst.) Period: 9/01/06 – 8/31/08 $50,000
Agency: NIH/NIDDKD Subcontract Type: Exploratory Research (R21-DK-077525-02)
The goal of this research subcontract with Benaroya Research Institute at Virginia Mason is to develop proteomic chips to detect HLA-A2*0201- and DRB1*0401- restricted islet antigen-specifc T cells.

Methods to study the CD4 T cell response to therapeutic proteins
Principal Investigator: Lawrence J. Stern Period: 8/15/06 - 8/15/07 $77,514
Sponsor: Wyeth Pharmaceuticals, Inc. Type: Sponsored Research Agreement
The goals of this sponsored research agreement are to develop methodology for identification of peptides responsible for driving CD4 responses to therapeutic proteins, and to establish methodology and collect data to help understand if there is a correlation between the level of CD4 response and the level of antibody response to therapeutic proteins.

Lipid-dependent folding and intracellular signaling by the T-cell receptor zeta chain cytoplasmic domain
Principal Investigator: Lawrence J. Stern Period: 9/01/02 – 2/28/05 $115,392
Agency: NSF BIO / MCB Type: Research Project (MCB1094264)
The major goal of this project is to determine the requirements, structural correlates, and functional role of a lipid-induced conformational change in the zeta subunit of the T cell receptor.

Structural studies of HIV nef and its interaction with the T cell receptor zeta subunit
Principal Investigator: Lawrence Stern Period: 7/01/03 – 6/30/04 $25,000
Agency: NIH / NIAID / CFAR Type: Center for AIDS Research (P30-AI42845)
The major goal of this project is to investigate aspects of HIV infection and pathogenesis through structural and biophysical studies of the interaction of the nef protein with the T cell receptor zeta subunit. This project is funded by a Developmental Grant for Evolving Research Opportunities from the UMass Center for AIDS research.

HIV-Derived Peptides as Class II MHC Antigens and Combinatorial Peptide Synthesis Facility
Project/core Leader: Lawrence J. Stern (Peter Kim, PI) Period: 8/1/97–7/31/02 $ 75,829
Agency: NIH / NIGMS Type: Program Project (PO1-GM56552)
The goals of this project are to determine the mode of binding of "non-conforming" HIV-derived antigenic peptides, and to design tight-binding peptide analogues that function as synthetic T-cell antigens. The core facility for combinatorial peptide synthesis is used by the Kim, Stern, and Williamson components of the program project.

Crystallization and Preliminary X-ray Diffraction Study of Human Serum Apolipoproteins
Principal Investigator: Lawrence J. Stern (A. Sigalov, Co-PI) Period: 9/1/97 – 12/31/99 $ 32,400
Agency: Civilian R&D Foundation Type: Research Project (CRDF-828)
This grant provided funds for a collaborator from the Independent States of the Former Soviet Union to visit the US to conduct experiments on the structural and functional consequences of apolipoprotein oxidation.

Summer Research in Macromolecular Interactions
Principal Investigator: Lawrence J. Stern Period: 5/1/01-3/31/05 $ 28,310
Sponsor: NIH / NIGMS Type: Training Grant (R25-GM62467)
This grant supports approximately ten summer undergraduate research projects in research groups throughout the department. The focus is on attracting students with a physical background into biomedical research. A collaboration with the University of Puerto Rico is intended to promote participation by underrepresented minority students.

Students and Trainees

Graduate students

Dikran Aivazian, MIT Biology Ph.D. 2001 (currently with Biogen-Idec, San Diego, CA)
Jennifer Cochran, MIT Chemistry Ph.D. 2000 (currently, Asst. Prof, Biomed. Eng. Stanford)
Gregory C. Carven, MIT Chemistry Ph.D. 2004 (currently with Phylogix, Waltham MA)
Thomas Cameron, MIT Chemistry Ph.D. 2002 (currently post-doc with M. Dustin, Skirball/NYU)
Ravi Joshi, MIT Health Sciences & Tech. M.D. 2000 (currently Asst. Prof. Medicine UCSF)
Walter Kim, UMass Ph.D./M.D. 2003-present
Venkatesh Murthy, MIT Chemistry S.M. 1996 (currently Fellow Cardiovasc Med, Harvard Med)
Tina Nguyen, UMass Biochemistry & Molecular Pharmacology, 2004-present
Corrie Painter, UMass Biochemistry & Molecular Pharmacology, 2004-present
Aaron Sato, MIT Chemistry 1994-1999, Ph.D. 1999 (now Sr. Director, Dyax Corp)
Zu-Ting Shen, UMass Immunology and Virology, 2005-present
Jennifer Stone, MIT Chem. Ph.D. 2006. (currently post-doc with D. Kranz, Univ. Illinois.
Peter Trenh, UMass Immunology and Virology, 2009-present
Liusong Yin, UMass Immunology and Virology, 2009-present
Jennifer Zarutskie, MIT Chemistry Ph.D. 2001 (now with Foley, Hoag, & Elliot, P.C.)
Zarixia Zavala-Ruiz, MIT Chem, Ph.D. 2004 (now Asst. Prof, Univ. Puerto Rico Mayaguez)

Undergraduate students

Lauren Angelo, Holy Cross College, 2003-2004
Helen Chan, MIT UROP, S.B. Chemistry 2000
Geeta Dayal, MIT UROP, 1998-1999
Stefan Karp, MIT UROP, 1996-1997
Jodi Lubetsky, MIT UROP, S.B. Chemistry 1996 (Ph.D. 2002 Yale)
Isaac Manke, Morehead State REU, Summer 1999 (currently MIT Ph.D. candidate)
Deepali Phadke, Northeastern Univ., Summer 1999, 2000.
Jennifer Svendson, MIT UROP, 1999-2000.

Post-doctoral associates

Carthene Bazemore-Walker, Ph.D. postdoc 1997-1999 (now Asst. Prof. Brown Univ.)
Mauricio Calvo-Calle, postdoctoral associate, 2006-present
Sriram Chitta, Ph.D., postdoctoral associate 2001-present.
Augustin de la Calle, Ph.D., postdoctoral associate, 1997-1998 (now with Exelixis Pharm.)
Walter Demkowicz, research scientist, 2004-2005 (now with BioVest)
Daniel DeOlivera, Ph.D., research scientist, 1998-2000 (now Sr. Scientist, Beaufor Ipsen)
Sarah Mortimer, Ph.D., postodoctoral associate, 2005-present
Maria-Dorothea Nastke, Ph.D., postdoctoral associate, 2007-present
Christian Parry, Ph.D., postdoctoral associate, 1998-2005 (now at NIH-NHLBI)
Carlos Parra-Lopez, M.D., visiting scientist, 2002, 2004 (now Assist Prof, Univ, of Bogota)
Sulabha Pathak, Ph.D., postdooc. assoc., 2000-2002 (currently at Tata Inst., Mumbai, India)
Efstratios Stratikos, Ph.D. postdoct. assoc. 2002-2004 (Researcher C, IIRP, Athens, Greece)
Alexander D. Sigalov, Ph.D., visiting scientist, 1997-1999, Senior Associate 2002-2006
Iwona Strug, Ph.D.postdoctoral associate, 2000-2006 (now Scientist, APT Biotech)
Prasanna Venkataraman, Ph.D. research scient, 2004-2006 (now Sci. Officer ATREC, India)

Doctoral Thesis committees

1994 Ramin Molloogababa (MIT)
1995 Pattie Christie, Richard Kosman (Harvard, Sc.M)
1996 Wing Hang Tong, Sherri Oslick, Charles Wescott, Patrick Zarrinker, Eric Meyer (MIT)
1997 Alex Brodsky, Matt Bogyo, Thomas Tolbert (MIT)
1998 Martha Rook, Jennifer Schmitke, Curtis Lockshin, Li Su, Tao Ke, Karen Sandman (MIT)

1999 Jason Haugh, Evan Powers, Kewen Kai, Eric Fallon, Eric Meyer, Ben Turk, Kelly Conway (MIT)
2001 Robert Doebele, Christopher Cilley, Kevin McDonnell, Tanya Williams (MIT)
2002 Justin Caravella (MIT), Jodi Lubetsky (Yale)
2003 Yueli Shen (Umass), Alexander Akheiser (MIT)
2004 Matthew Anderson (Univ. Wisc.), Balaji Rao (MIT)
2005 Shayln Clute (UMass), Shahram Misaghi (Harvard)
2006 Charles Town (UMass), Jennifer Foulkes-Murzycki (UMass, PhD-MD)
2007 Evan Jellison (UMass)
2008 Martin Felices, Nitya Jain (UMass)
2009 Qi Wu (UMass, S.M.)

Teaching and Education

UMass Medical School and Graduate School of Biomedical Sciences

IM770 Molecular and Cellular Immunology I (coordinator, Spring 2004-2008)
This course provides students with a working knowledge of the immune system and the specialized vocabulary that describes it. Topics include the structure, function and genetics of immunoglobulins, T lymphocyte antigen receptors, and MHC proteins; the development and differentiation of lymphocytes, cell-cell interactions in the immune system, and the regulation of immune responses. In 2004 Dr. Stavnezer and I reformatted the course to include more in class discussion and more problem solving practice, together with an increase in credit hours. In addition to coordinating the course I am responsible for lectures on Immunological Concepts, Induction of Adaptive Immune Responses, Antibody Structure and Antigen Recognition, and MHC Proteins and Antigen Presentation.

BP717 Protein Crystallography (Spring 2004,2006, 2008)
This course teaches the fundamentals of macromolecular crystallography theory and practice. I am responsible for lectures on Molecular Replacement and Real Space Methods

Immunology Small Groups (Fall 2004-2008)
This small group discussion session helps medical students to understand the relationship between their lecture material on immunological topics and case studies involving lymphoma, leprosy, lupus, and diabetes

MS614 Biomedical Sciences II and III (Spring 2003, Fall 2004-2008)
This course is taught as series of lectures and conferences presenting the principles of the sciences basic to medicine. I was responsible for RAPS literature discussion sections on Immune Responses, Membrane Proteins, and Protein-Ligand Interactions

Ph.D. / M.D. tutorial (Walter Kim, 2003, Connie Lee 2004)
PhD/MD students enroll in a one-on-one tutorial with a faculty member they select each semester during their pre-clinical years. Consisting of one hour per week, this tutorial facilitates integration between the medical and graduate school curricula.

Invited Talks

National Jewish Center for Immunology, Denver, July 1994
American Association of Clinical Immunologists, Cambridge MA, July 1994
Frontiers in Chemistry, MIT Independent Activities Period, January 1995
U. Mass. Medical School, Pharmacology Department, March 1995
Peptidomimetics and Small Molecule Design, Philadelphia, March 1995
Princeton University, Chemistry Department, May 1995
Ninth International Congress of Immunology (workshop chair), San Francisco, July 1995
American Chemical Society, Biophysical Chemistry Section, Chicago, August 1995
American Society for Histocompatibility and Immunogenetics, Dallas, October 1995
First International Workshop on Antigen Processing and Presentation, Oxnard CA, December 1995
QEM/MIT President's Technology Conference, Computers in Chemistry, MIT, January 1996
Center for Advanced Research in Biotechnology (NCI), Univ. Maryland, March 1996
CAREER conference, National Science Foundation, June 1996
Johns Hopkins Medical University, Department of Pathology, February 1997
Institute de Recherches Cliniques de Montreal (IRCM) and McGill University, April 1997
Brandeis University, Department of Biochemistry, May 1997
Pfizer Inc, Central Research Division, Groton CT, January 1998
Keystone Conference "T-cell activation, differentiation, and death," Keystone CO, January 1998
Structural Biology Section, NIAID, NIH, January 1999
Syracuse University, Department of Chemistry, February 1999
Blood Research Center of Southern Wisconsin, Milwaukee, February 1999
Northwestern University, Department of Biochemistry, Mol. Biol., and Cell. Biol., March 1999
Oxford University, Institute for Molecular Medicine, July 1999
University College, London, Departments of Immunology and Pathology, July 1999
6th International Conference on Langerhans Cells, New York, October 1999
2nd International Meeting on Antigen Processing and Presentation, Bar Harbor ME, October 1999
Boston University School of Medicine, Department of Biophysics, Boston MA, December 1999
University of North Carolina Medical School, Dept of Microbiology and Immunology, April 2000
NIH Annual Tetramer Facility Meeting, Seattle WA, May 2000
American Association of Immunologists, Session Chair, Seattle WA, May 2000
Stanford University, Department of Immunology, Palo Alto CA, May 2000
ASBMB Symposium: Chemical approaches to modulating cellular processes, Boston MA, June 2000
International Symposium on Nucleic Acids and Signal Transduction, Brandeis Univ., July 2000.
Dana-Farber Cancer Institute, Department of Cancer Immunology and AIDS, September 2000
Scripps Research Institute, Department of Chemistry, September 2000
California Institute of Technology, Department of Chemistry, September 2000
University of Edinburg, Department of Chemistry, Scotland, September 2000
Imperial Cancer Research Fund, London, Immunobiology Section, October 2000
Roche Institute of Immunology, Basel, Switzerland, October 2000
Institut National de la Santé et de la Recherche Médicale (INSERM), Ctr. for Biomed. Res., Paris, Oct. 2000
Cornell University, Department of Molecular Biology and Genetics, October 2000
Sloan-Kettering Institute, Department of Immunology, January 2001
National Science Foundation, Molecular and Cellular Biosciences, April 2001.
University of Massachusetts Medical School, Department of Pathology, May 2001.

MHC database planning meeting, NIH/NCBI/NIAID, June 2001
Johns Hopkins Medical Institute, Department of Biological Chemistry, September 2001
Tufts University Medical School, Department of Pathology, October 2001
Johns Hopkins School of Public Health, Dept. of Molecular Microbiology and Immunology, Oct 2001
Kimmel Cancer Institute, Thomas Jefferson School of Medicine, Philadelphia PA, September. 2001
Yale University School of Medicine, Section of Immunobiology, November 2001.
The Blood Research Institute, Milwaukee WI, December 2001
U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), Fort Detrick, MD, Dec. 2001.
National Institutes of Health, Class II Tetramer Workshop, Bethesda MD, July 2002
Mathematics and Network Theory, Notre Dame University, South Bend IN, August 20002
Third International Meeting on Antigen Processing and Presentation, Paris France, May 2002
Fifth Efis International TATRA Immunology Conference, Tatranské Zruby, Slovakia, September 2002
New York University School of Public Health, Department of Parasitology, March 2003
Blood Research Institute, Milwaukee WI, March 2004
Albert Einstein College of Medicine, Department of Pathology, March 2004
Stanford University Medical College, Department of Immunology, April 2004
Fourth International Congress on Nucleic Acids and Membranes, Okayama, Japan, October 2004
Boston Biomedical Research Institute, March 2005
University of Massachusetts Amherst, Department of Molecular and Cellular Biology, March 2005.
Wyeth Vaccine Research Center, Pearl River, NY, Aug 2005.
Protein Research in the "Omics" and Biotechnology Era Conference, San Juan P.R., March 2006.
Johns Hopkins Univ. School of Medicine, Program in Immunology, Baltimore May 2006
Wyeth BioPharma, Cambridge NY, July 2006
MHC Tetramers Today and Tomorrow Workshop, Bethesda Nov 2006.
Immunology 2007, American Association of Immunologists Annual Meeting, Miami, Fl, May 2007
Burnet Institute for Medical Research, University of Melbourne, Australia, September 2007
Antigen Presentation 2007, Dunk Island, Australia, October 2007
3rd International Conference on Beryllium Disease, Plenary Lecture, October 2007
Massachusetts General Hospital East, Boston, December 2007
Tulane University Health Sciences Center, Department of Biochemistry, March 2008
Brown University Department of Chemistry, April 2009.